REMARKS

Claim 9 is pending in the instant application. Claim 9 has been rejected. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

I. Rejection of Claims Under 35 U.S.C. §103

Claim 9 has been rejected under 35 U.S.C. §103(a) as being unpatentable over Moyer et al. ((Aug. 1999) *Am. J. Physiol.* 277(2 Pt 2):F271-6) in view of Cormack et al. ((1996) *Gene* 173:33-38) further in view of Chou et al. (1991) *J. Biol. Chem.* 266:24471-24476). The Examiner suggests that Moyer et al. teach a method of measuring the effect of butyrate on expression of a CFTR-GFP nucleic acid and the use of CFTR with the deltaF-508 mutation in the method. It is acknowledged that Moyer et al. do not teach using a nucleic acid construct comprising CFTR and eGFP; however, it is suggested that Cormack et al. teach mutants of GFP which fluoresce more intensely than wild-type GFP. It is further suggested that while Moyer et al. and Cormack et al. do not teach the use of the proximal human CFTR promoter, Chou et al. teach the transcription regulatory elements of the CFTR gene including a proximal, positive element delimited by the 5′ deletion constructs -226 base pairs upstream of the transcription start site. The Examiner suggests that it would have been obvious to one of skill in the art at the time the invention was made to practice a method for identifying agents which increase functional cell surface expression of the deltaF-508 CFTR protein by exposing cells comprising a genetic

construct comprising human CFTR coding sequence and a reporter gene to the agent, measuring expression levels or trafficking of CFTR to the membrane, and comparing the levels of CFTR expression or trafficking to controls as taught in Moyer et al., wherein the reporter gene is eGFP as taught by Cormack et al., and the promoter used is the CFTR promoter as taught by Chou et al. The Examiner suggests that motivation is provided by Cormack et al. in the teaching that eGFP has greatly enhanced fluorescence intensity and by Chou et al. in teaching that the promoter of the CFTR can be used to obtain insights into the mechanisms governing the regulation of CFTR expression. Applicants respectfully traverse this rejection.

At the outset, Applicants respectfully point out that the Moyer et al. do not teach or suggest the use of a nucleic acid construct encoding ΔF508 CFTR-GFP in the method disclosed therein. This reference teaches at page F271 (second column, lines 2-13) that butyrate and its analogs are useful for the treatment of cystic fibrosis in individuals expressing ΔF508 CFTR because these agents stimulate expression of ΔF508 CFTR, plasma membrane localization of ΔF508 CFTR, and cAMP-activated Cl^- secretion in nasal, bronchial, and pancreatic epithelial cells. To address the effect of butyrate on Cl^- secretion in renal epithelial cells, Moyer et al. employed a GFP-CFTR construct to monitor CFTR expression and localization. Throughout the "METHODS" section at pages F271 and F272 and the "RESULTS" section at pages F272 to F274, Moyer et al. describe the analysis of MDCK cells stably transfected with the GFP-CFTR construct with no teaching or suggestion of a ΔF508 CFTR-GFP construct. Moreover, Moyer et al.

contrast their findings concerning GFP-CFTR expression and activity in renal cells exposed to butyrate with the expression and activity of ΔF508 CFTR in cystic fibrosis epithelial cells treated with butyrate, concluding that clinical use of butyrate may be useful for treating cystic fibrosis, but may actually compromise *wild-type CFTR function in kidney epithelia*. See page F275, column 2, lines 7-15 and second full paragraph. Thus, in contrast to the Examiner's suggestion, Moyer et al. do not teach or suggest a genetic construct comprising a mutant human CFTR cDNA for use in a method of measuring the effect of butyrate on expression of a CFTR-GFP because the only construct disclosed by Moyer et al. was wild-type CFTR-GFP. In so far as Cormack et al. teach mutant GFP and Chou et al. teach transcriptional regulatory elements of CFTR, these references fail overcome the deficiencies in the teachings of Moyer et al.

MPEP 2143.03 states that to establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. In re Royka, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). The cited references fail to meet this requirement because when combined, Moyer et al., Cormack et al. and Chou et al. fail to teach or suggest the use of a mutant human CFTR cDNA coding region and a cDNA of an EGFP reporter gene linked at the 5′ end to the mutant human CFTR cDNA coding region and wherein said cDNAs are under the regulation of the proximal human CFTR promoter region. Thus, it is respectfully requested that this rejection be reconsidered and withdrawn.

II. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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